

Amendments to the Drawings:

The attached 12 sheets of drawings include changes to Figs. 2, 6A-7:

Replacement Sheets 2/19-3/19 (Fig. 2), replace originally submitted sheets 2/19-3/19 (Fig. 2).

Replacement Sheets 7/19-13/19 (Figs 6A-6D), replace originally submitted sheets 7/19-13/19 (Figs. 6A-6D).

Replacement Sheets 14/19-16/19 (Fig. 7), replace originally submitted sheets 14/19-16/19 (Fig. 7).

The Amendments to the Drawings are made to incorporate the sequence identifier numbers. Applicant has submitted a "Marked-up" version of original sheets 2/19-3/19 and 7/19-16/19.

Attachment: 24 sheets of drawings, i.e., 12 "Replacement" and 12 "Marked-Up" sheets of drawings.

REMARKS


Applicants submit that the substitute specification and replacement drawings are filed simply to incorporate the sequence identifier numbers. No new matter is added.

Applicant submits that all claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicant's attorney/agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney/agent of record.

Date:

3-30-2005

Respectfully submitted,



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MARKED-UP VERSION

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FIGURE 2

Score = 553 bits (1425), Expect = e-156
Identities = 327/700 (46%), Positives = 406/700 (57%), Gaps = 152/700 (21%)



Query: 1
Sbjct: 1
Beta-strand region 50
Hydrogen bonded turn 48
Beta-strand region 41
Hydrogen bonded turn 38
Beta-strand region 28
Hydrogen bonded turn 26
Helical region 13
Beta-strand region 7
SH2 1. 6
Hydrogen bonded turn 5
PTPN11 1

MSSRRWFHPTISGIEAEKLLQEQQGFDGSLARLSSSNPGAFTLVRRGNEVTHIKIQNNG 60
M+SRWFHP I+G+EAE LL +G DGSFLAR S SNPG FTLVRR VTHIKIQN G
MTSRRWFHPNITGVEAENLLLTRGVDGSLARPSKSNPGDFTLVRRNGAVTHIKIQNTG 60

(SEQ ID NO:279)

(SEQ ID NO:280)

Query: 61
Sbjct: 61
Hydrogen bonded turn 83
Helical region 74
Beta-strand region 70
Hydrogen bonded turn 66
Beta-strand region 63
SH2 1. 61
PTPN11 61
Hydrogen bonded turn 85
Helical region 119
Beta-strand region 113
SH2 2. 112
Hydrogen bonded turn 111
Hydrogen bonded turn 108
Beta-strand region 100
Beta-strand region 95
Beta-strand region 89

61 DFFDLYGGEKFPATLPELVQYYMEN-GELKEKNGQAIELKQPLICAEPPTERWFHGNLSGK 119
D++DLYGGEKFPATL ELVQYYME+ G+LKEKNG IELK PL CA+PT+ERWPHG+LSGK
DYYDLYGGEKFPATLAEVLQYYMEHGHQLKEKNGDVIELKYPLNCADPTSERWFHGHLSGK 120

Query: 120
Sbjct: 121
Beta-strand region 147
Hydrogen bonded turn 144
Beta-strand region 134
Hydrogen bonded turn 132
Hydrogen bonded turn 129
Helical region 121
SH2 2. 121
PTPN11 121
Beta-strand region 178
Hydrogen bonded turn 176
Beta-strand region 166

120 EAEKLILERGKNGSFLVRESQSKPGDFVLSVRTD-----KVTHVMIRWQDKKYD 169
EAEKL+ E+GK+GSFLVRESQS PGDFVLSVRT D KVTHVMIR Q+ KYD
121 EAEKLLTEKGKHSFLVRESQSHPGDFVLSVRTGDDKKGESNDGKSKVTHVMIRQELKYD 180

Query: 170
Sbjct: 181
Helical region 223
Beta-strand region 221
Beta-strand region 214
Beta-strand region 209
Hydrogen bonded turn 205
Beta-strand region 203
Helical region 190
Beta-strand region 187
PTPN11 181
SH2 2. 181
Helical region 226

170 VGGGESFGTLSELIDHYKRNPMVETCGTVVHLRQPFNATRITAAGINARVEQLVKGGFWE 229
VGGGE F +L++L++HYK+NPMVET GTV+ L+QP N TRI A A +E V+
181 VGGGERFDSLTDLVEHYKKNPMVETLGTVLQLKQPLNTRINA----AEIESRVR----- 231

Query: 230
Sbjct: 232
Helical region 266
Helical region 256
Helical region 247
PTPN11 232
Helical region 232

230 EFESLQQDSRDTPSRNEGYKQENRLKNRYRNILPYDHTRVKLLDVEHSVAGAEYINANYI 289
L + + T +G+ +E + L Y
232 ---ELSKLAETTDKVKQGFWEFETLQQQECKLLYSRKE----- 267

Query: 290
RLPTDGDLYNMSSSSSLNSSVSPCPACTAAQTQRNCSNCQLQNKTCVQCAVKSAILPYS 349
Q Q N + + +N ILP+

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Sbjct: 268 -----GQRQENKKNRYKN-----ILPPD 286
Hydrogen bonded turn 280
PROTEIN-TYROSINE PHOSPHATASE. 276
Helical region 271
PTPN11 268
Helical region 268
Hydrogen bonded turn 286

Query: 350 NCATCSRKSDSLSKHKRSESSASSPSSGSGSGPGSSGTSGVSSVNGPGTPTNLTSCTAG 409
      + D P P +
Sbjct: 287 HTRVVLHDGD-----PNEPVS----- 302
Beta-strand region 289
Hydrogen bonded turn 287
PTPN11 287
PROTEIN-TYROSINE PHOSPHATASE. 287

Query: 410 CLVGLLKRHSNDSSGAVSISMAERERE-REREMFKTYIATQGCLLTQQVNTVTDVFNMMVW 468
      D A + I M E E + + K+YIATQGCL NTV DFW MV+
Sbjct: 303 -----DYINA-NIIMPEFETKCNNSKPKSYIATQGCLQ-----NTVDFWRMV 346
Beta-strand region 304
PTPN11 303
PROTEIN-TYROSINE PHOSPHATASE. 303
Hydrogen bonded turn 335
Beta-strand region 327
Helical region 338

Query: 469 QENTRVIVMTTKEYERGKEKCARYWPDEGRSEQFGHARIQCVSENSTSDYTLREFLVSWR 528
      QEN+RVIVMTTKE ERGK KC +YWPDE ++G R++ V E++ DYTLRE +S
Sbjct: 347 QENSRVIVMTTKEYERGKSKCVKYWPDEYALKEYGVMVRNVKESAAHDYTLRELKLSKV 406
Hydrogen bonded turn 406
Beta-strand region 396
Beta-strand region 383
Hydrogen bonded turn 381
Beta-strand region 377
Hydrogen bonded turn 374
Beta-strand region 364
Hydrogen bonded turn 362
Beta-strand region 360
Beta-strand region 352
Hydrogen bonded turn 349
Helical region 347
PTPN11 347
PROTEIN-TYROSINE PHOSPHATASE. 347

Query: 529 DQ--PARRIFHYHFQVWPDHGVDPADPGCVLNFQLQDVNTRQSHLAQAGEKPGPICVHCSAG 586
      Q R ++ YHF+ WPDHGV+DPG VL+FL++V+ +Q + AG P+ VHCSAG
Sbjct: 407 GQGNTERTVQYHFTWPDHGVPSDPPGGVLDLFEEVHHKQESIMDAG---PVVVHCSAG 462
Beta-strand region 408
Hydrogen bonded turn 407
PTPN11 407
PROTEIN-TYROSINE PHOSPHATASE. 407
Hydrogen bonded turn 450
Helical region 432
active 459
Beta-strand region 455

Query: 587 IGRGTGFIVIDMILDQIVRNGLDTEIDIQRTIQMVRQSRLVQTEAQYKFVYVAVQHYI 646
      IGRGTGFIVID+++D I G+D +ID+ +TIQMVRQSRLVQTEAQY+P+Y AVQHYI
Sbjct: 463 IGRGTGFIVIDILIDIIREKGVDCDIDVPKTIQMVRQSRLVQTEAQYRFIYMAVQHYI 522
Helical region 508
Hydrogen bonded turn 502
Hydrogen bonded turn 499
Helical region 490
Beta-strand region 487
Hydrogen bonded turn 484
Helical region 464
PTPN11 463
PROTEIN-TYROSINE PHOSPHATASE. 463

Query: 647 QTLIARKRAEEQSLQVGREYTNIKYTGEIGNDSQRSPLPP 686
      +TL R E++S + G EYTNIKY+ +SPLPP
Sbjct: 523 ETLQRRIEEEQSKRKGEYTNIKYSLADQTSQDQSPPLPP 562
Conflict 548
phosphorylation 542
Conflict 535
Hydrogen bonded turn 524
Helical region 523
PTPN11 523

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MARKED-UP VERSION

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FIGURE 6A

Sequence alignment of Dros Dlg1 and Hu Dlg homolog 1

BLAST P sequence alignment

Score = 616 bits (1588), Expect = e-175
Identities = 306/517 (59%), Positives = 390/517 (75%), Gaps = 24/517 (4%)

Query: 453 QPGSRYASTNVLAAPPPTPRAVST-----EDITREPTITIQKGPQGLGFNIVGGE 504
QP + S + P + P S ++ITREPR + + +G GLGFNIVGGE
Sbjct: 425 QPVDNHVSPSSFLGQTPASPARYSFVSKAVLGDDDEITREPRKVVLRHGSTGLGFNIVGGE 484

Query: 505 DGQGIYVSFILAGGPADLGSSELKRGDQLLSVNNVNLTHATHEEAAQALKTSGGVVTLAQ 564
DG+GI++SFILAGGPADL EL++GD+++SVN+V+L A+HE+AA ALK +G VT++AQ
Sbjct: 485 DGEFIFISFILAGGPADLSELKRGDRIISVNSVDLRAASHEQAAAALKNAGQAVTIVAQ 544

Query: 565 YRPEEYNRFEARIQELKQXXXXXXXXXXXX-XXQKRSLYVRALFDYDPNRDDGLPSRG 623
YRPEEY+RFEA+I +L++Q QKRSLYVRALFDYD +D GLPS+G
Sbjct: 545 YRPEEYSRFEAKIHDLREQMNSSISSGSGSLRTSQKRSLYVRALFDYDKTKDSGLPSQG 604

Query: 624 LPFKHGDILHVTNASDDEWQARRVLGDNEDEQIGIVPSKRRWERKMRARDRSVKFQGHA 683
L FK GDILHV NASDDEWQAR+V D E +++G++PSKRR E+K RAR ++VKF
Sbjct: 605 LNFKPGDILHVINASDDEWQARQVTPDGESDEVGVIPSKRRVEKKERARLKTVKFN--- 661

Query: 684 AANNLNDKQSTLDRKKKNFTFSRKFPFMKSDEKNEDEGSDQEPNGVVSSTSEIDIXXXX 743
+ DK + + K+K FSRKFPF K++D+ ++ SD + + V S+ S+ +
Sbjct: 662 --SKTRDKQSFNDKRRKNLFSRKFFYKNDQSEQETSADQHVTSNASDSE----- 712

Query: 744 XXXXXXXXXXXXXVLSYEAQRLSINYTRPVIIILGPLKDRINDDLISEYDPKFGSCVPHTT 803
VLSYE V + +NYTRPVIIILGP+KDRINDDLISE+PDKFGSCVPHTT
Sbjct: 713 ---SSYRGQEYVLSYEPVNNQEVNYTRPVIIILGPMKDRINDDLISEFPDKFGSCVPHTT 769

Query: 804 RPKREYEVDRDYHFVSSREQMERDIQNHLEAGQYNDNLYGTSVASVREVAEKGHCI 863
RPKR+YEVDGRDYHFV+SREQME+DIQ H FIEAGQYN++LYGTSV SVREVA KGHCI
Sbjct: 770 RPKRDYEVDRDYHFVTSREQMEKDIQEHKFIAGQYNNHLYGTSVQSVREVAGKGHCI 829

Query: 864 LDVSGNAIKRLQVAQLYPVAVFIKPKSVDSVMEMNRRMTEEQAKKTYERAIKMEQEFGEY 923
LDVSGNAIKRLQ+AQLYP+++FIKPKS++++MEMN+R+TEEQA+KT+ERA+K+EQEF E+
Sbjct: 830 LDVSGNAIKRLQIAQLYPISIFIKPKSMENIMEMNKRLTEEQARKTFERAMKLEQEFTEH 889

Query: 924 FTGVVQGDTEIEIYSKVKSMIWSQSGPTIWPVSKESL 960
FT +VQGDTE+IY++VK +I QSG IWVP+KE L
Sbjct: 890 FTAIVQGDTELDIYNQVKQIEEQSGSYIWPVPAKEKL 926

Score = 206 bits (524), Expect = 2e-51
Identities = 119/227 (52%), Positives = 146/227 (63%), Gaps = 30/227 (13%)

(SEQ ID NO:281)

(SEQ ID NO:282)

(SEQ ID NO:283)

(SEQ ID NO:284)

Query: 24 LFNLDSE-----VNGDDSEWLYEDIQLERGNGLGFSIAGGTDNPHIGTDTSIYITKLIS 76
L N DS VNG D+ + YE+I LERGNGLGFSIAGGTDNPHIG D+SI+ITK+I+
Sbjct: 201 LVNTDSLETPTYVNGTDADYEYEBITLERGNGLGFSIAGGTDNPHIGDDSSIFITKIIT 260

Query: 77 GGAAAADGRLXXXXXXXXXXXXXXXXXPHASAVDALKKAGNVVVLHVKKRXXXXXXXXXXXX 136
GGAAA DGRL H+ AV+ALK+AG++V+L+VKR+
Sbjct: 261 GGAAAQDGLRLRVNDCILQVNEVDVRDVTHTSKAVEALKEAGSIVRLYVKKRKPVSSE----- 315

Query: 137 XXXXXXXXXXXXXXXKVIEIDLKVGKGLGFSIAGGIGNQHIPGDNGIYVTKLTDGGRAQV 196

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Sbjct: 316 -----KIMEIKLIKPKGLGFSIAGGVGNQHIPGDN SIYVTKIIEGGAHK 361

Query: 197 DGRLSIGDKLIAVRTNGSEKNLENVTHELAVATLKSITDKVTLIIGK 243
 DG+L IGDKL+AV + LE VTHE AV LK+ +D V L + K

Sbjct: 362 DGKLQIGDKLLAV---NNVCLEEVTHEEAVTALKNTSDFVYLKVAK 404

Score = 88.2 bits (217), Expect = 7e-16

Identities = 68/234 (29%), Positives = 95/234 (40%), Gaps = 43/234 (18%)



Query: 40 DIQLERGNISGLGFSIAGGTDPHIGTDTSIYITKLISGAAAADGRLXXXXXXXXXXXXX 99
 +I+L +G GLGFSIAGG N HI D SIY+TK+I GGAA DG+L

Sbjct: 319 EIKLIKGPGLGFSIAGGVGNQHIPGDN SIYVTKIIEGGAHKDKLQIGDKLLAVNNVC 378

Query: 100 XXXXPHASAVDALKKAGNVVVLHVVRKXXXXXXXXXXXXXXXXXXXXXXXXXVI----- 153
 H AV ALK + V L V + V

Sbjct: 379 LEEVTHEEAVTALKNTSDFVYLKVAKPTSMYNDGYAPPDITNSSSQPVDNHVSPSSFLG 438

Query: 154 -----EIDLKVGKGLGFSIAGGIGNQHIPGDN SIYVTKIIEGGAHKDKLQIGDKLLAVNNVC 378
 ++ L +G GLGF+I GG + GI+++

Sbjct: 439 QTPASPARYSPVSKAVLGDDEITREPRKVVLRHGSTGLGFNIVGGEDGE-----GIFIS 492

Query: 187 KLTGGRQAQVDGRLSIGDKLIAVRTNGSEKNLENVTHELAVATLKSITDKVTLI 240
 + GG A + G L GD++I+V + +L +HE A A LK+ VT++

Sbjct: 493 FILAGGPADLGSGLRKGDRISV---NSVDLRAASHEQAAAALKNAGQAVTIV 542

Score = 70.1 bits (170), Expect = 2e-10

Identities = 47/141 (33%), Positives = 69/141 (48%), Gaps = 12/141 (8%)



Query: 432 MPALPVESNQTNNSQSPPQPGSRVASTNVLAAPPPTPRAVSTEDITREPTITIQK 491
 +P LPV + T PQ P +T+ L TP V+ D E IT+++

Sbjct: 176 IPVLPVPAENTVILPTIPQANPPPV-LVNTDSLE-----TPTYVNGTDADYEYEEITLER 229

Query: 492 GPQGLGFNIVGGEDG-----QGIYVSFILAGGPADLGSSELKRGDQLLSVNNVNLTHATH 545
 G GLGF+I GG D I+++ I+ GG A L+ D +L VN V++ TH

Sbjct: 230 GNSGLGFSIAGGTDPHIGDDSSIFITKIITGGAAQDGRRLRVNDCILQVNEVDVRDVTH 289

Query: 546 EEAAQALKTSGGVVTLAQYR 566
 +A +ALK +G +V L + R

Sbjct: 290 SKAVEALKEAGSIVRLYVKRR 310

Score = 67.4 bits (163), Expect = 1e-09

Identities = 39/81 (48%), Positives = 49/81 (60%), Gaps = 6/81 (7%)



Query: 487 ITIQKGPQGLGFNIVGGEDGQ-----GIYVSFILAGGPADLGSSELKRGDQLLSVNNVNL 540
 I + KGP+GLGF+I GG Q IYV+ I+ GG A +L+ GD+LL+VNNV L

Sbjct: 320 IKLIKGPGLGFSIAGGVGNQHIPGDN SIYVTKIIEGGAHKDKLQIGDKLLAVNNVCL 379

Query: 541 THATHEEAQALKTSGGVVTL 561

THEEA ALK + V L

Sbjct: 380 EEVTHEEAVTALKNTSDFVYL 400

(SEQ ID NO:285)

(SEQ ID NO:286)

(SEQ ID NO:287)

(SEQ ID NO:288)

(SEQ ID NO:289)

(SEQ ID NO:290)

MARKED-UP VERSION

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FIGURE 6B

CLUSTAL W (1.82) sequence alignment

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Drosophila  MTTRKKKRDGGGSGGGFIKKVSSLFNLDVNGDDSWLYEDIQLERGNLGLFSIAGGTDN 60
Human      MPVRKQD-----TQRALHLLLEYRSKLSQTEDRQLRSSIERVINIFQSNLFQ 47
          *..**:. . . :.* . . . ** ** . . . : : . . :

Drosophila  PHIGTDTSIYITKLISGGAAADGRLSINDIIVSVNDVSVVDVPHASAVDALKKAGNVVK 120
Human      ALIDIQEFYEVTLTDN--PKCID-RSKPSEPIQPVNTWEISSLPSTVTSETLPSSLSPS 104
          . * . : : * * . . . * . . : * ** . : . : * : . . . : . .

Drosophila  LHVKRKRGTATTAAAGSAAGDARDAASAGPKVIEIDLKGGKGLGFSIAGGIGNQHHPGD 180
Human      VEKYRYQDEDTPPQEHISP--QITNEVIGPELVHVSEKN--LSEIENVHGFVSHSHIS-P 159
          :. * :. *. * :. . . **::: . : . . : * :. :. **.

Drosophila  NGIYVTKLTDGGRAQVDGRLSIGDKLIAVRTNGSEKN---LENVTHELAVATLKSITDKV 237
Human      IKPTEAVLPSPTVPVPIVLPVPAENTVILPTIPQANPPVPLVNTDSLETPTYVNGTDAD 219
          : *.. . * * . : : : . . . : * : *..* . . . **

Drosophila  TLIIGKTQHLTTSAS---GGGGGGLSSGQQLSQSQSQLATSQSQSQVHQQQHATPMVNS 293
Human      YEYEEITLERGNLGLFSIAGGTDNPHIGDDSSIFITKIITGGAAQDGRLRVNDCILQV 279
          * . *. . ** .. *: * : : * . : * : : : :

Drosophila  QSTGALNSMGQTVDSPSIPQAAAAVAAAANASASASVIASNNNTISNTTVTVTATATAS 353
Human      NEVDVRDVTHTSKAVEALKEAGSIVRLYVKKRKPVSEKIMEIK-LIKGPKGLGFSIAGGVG 338
          : . . . : . . * : : . . : . . . * : : : * . . . : : . .

Drosophila  NDSSKLPPLSGANSSISISNSNSNSNSNNINNINSINNNSSSSSTTATVAAATPTAASA 413
Human      NQHIPGDNISYVTKIIEGGAHKGDKLQIGDKLLAVNNVCLEEVTHEEAVTALKNTSDFV 398
          *: * : . . * . . : : : : : : : : : : : : : : : : : :

Drosophila  AAAAASSPPANSFYNNASMPALPVESNQTNRSQSPQPRQPGSRYASTNVLAAPPGTTPR 473
Human      YLKVAK-PTSMYMNDGYAPPDITNSSSQPVDNHVSPSS-FLGQTPASP--ARYSPVSKA 453
          . * . * : : : * : . *. * . . . ** . * . ** . * . * :

Drosophila  AVSTEDITREPRITIQKGPQGLGFNIVGGEDGQGIYVSFILAGGPADLGSSELKRGDQLL 533
Human      VLGDEITREPRKVVLRHGSTGLGFNIVGGEDGEGIFISFILAGGPADLGSSELKRGDRII 513
          : . : : : : : : : : : * . : : : : : : : : : : : : : : : : : :

Drosophila  SVNNVNLTHATHEEAAQALKTSGGVVTLLAQYRPEEYNRFEARIQELKQQAALGAGGSGT 593
Human      SVNSVDLRAASHEQAAAALKNAGQAVTIVAQYRPEEYSRFEAKIHDLREQMMNSSISSGS 573
          ***. : * : : * : * * . : * . : : : : : : : : : : : : : : : : : :

Drosophila  -LLRTTQKRSLYVRALFDYDPNRDDGLPSRGLPFKHGDILHVTNASDDEWWQARRVLGDN 652
Human      GSLRTSQKRSLYVRALFDYDKTKDGLPSQGLNFKFGDILHVINASDDEWWQARQVTPDG 633
          ***: : : : : : : : : : * . : : : : * * . : : : : : : : : : : * .

Drosophila  EDEQIGIVPSKRRWERKMRARDSVKFQGHAAANNLQKSTLDRKKKNFTFSRKFPFMK 712
Human      ESDEVGVIPSKRRVEKKERARLKTVKFN----SKTRDKGQSFNDKRRKNLFSRKFPFYK 688
          * . : : : : : : : : * : * * : : : : : . . * . : : : * : * : : : *

Drosophila  SRDEKNEDGSDQEPNGVVSSTSEIDINNVMNNQSNQEPQSEENVLSYEAVQRLSINYTRP 772
Human      NKDQSEQETSDADQH-VTSNASDSESSYRQ-----EYVLSYEPVNNQEVNYTRP 738
          . : * : : : * * : : * . : * : : . . : : * * * * * . : : : : * *

Drosophila  VIILGPLKDRINDDLISEYDPKFGSCVPHTTRPKREYVDGRDYHFVSSREQMERDIQN 832
Human      VIILGPMKDRINDDLISEFPDKFGSCVPHTTRPKRDYVDGRDYHFVTSREQMEKDIQEH 798
          * * * * * : * * * * * : : : : : * * * * * : : : : : * * * * * : * * :

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(SEQ ID NO:291)
(SEQ ID NO:267)

MARKED-UP VERSION

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Drosophila LFIEAGQYNDNLYGTSVASVREVAEKGKHCILDVSGNAIKRLQVAQLYPVAVFIKPKSVD 892
Human KFI EAGQYNNHLYGTSVQSVREVAGKGKHCILDVSGNAIKRLQIAQLYPISIFIKPKSME 858
 *****;:***** ***** *****;*****;:*****;:

Drosophila SVMEMNRRMTTEEQAKKTYERAIKMEQEFGEYFTGVVQGD TIEEIYSKVKSMIWSQSGPTI 952
Human NIMEMNKRLTEEQARKTFERAMKLEQEFTEHFTAIVQGD TLEDIYNQVKQIIEEQSGSYI 918
 .:*****:*:*****:***:***:*:***** *:**.:*****:***:***:*. * .****. *

Drosophila WVPSKESL 960
Human WVP AKEKL 926
 :.*


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FIGURE 6C

Sequence alignment of Dros Dlg1 and Hu Dlg homolog 2

BLASTP sequence alignment

Score = 621 bits (1601), Expect = e-176
Identities = 318/524 (60%), Positives = 390/524 (73%), Gaps = 43/524 (8%)



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Query: 438 ESNQTNNRSQSPQPRQPGSRYASTNVLAAPPPTPRAVSTEDITREPTITIQKGPQGLG 497
      +S T++ S RQP RAVS E EPR + + KG GLG
Sbjct: 389 DSEMTSHSQHSTATRQPSMTLQ-----RAVSLEG---EPRKVV LHKGSTGLG 432

Query: 498 FNIVGGEDGQGIYVSFILAGGPADLGSSELKRGDQLLSVNNVNLTHATHEEAAQALKTSGG 557
      FNIVGGEDG+GI+VSFILAGGPADL EL+RGDQ+LSVN ++L A+HE+AA ALK +G
Sbjct: 433 FNIVGGEDGEGIFVSFILAGGPADLSELQRGDQILSVNGIDLRGASHEQAAAALKGAGQ 492

Query: 558 VVTLAQYRPEEYNRFEARIQELKQXXXXXXXXXXXXXXXXX-QKRSLYVRALFDYDPNRD 616
      VT++AQY+PE+Y RFEA+I +L++Q QKRSLYVRA+FDYD ++D
Sbjct: 493 TVTIIAQYQPEDYARFEAKIHDLREQMMNHSMSGSGSLRTNQKRSLYVRAMFDYDKSKD 552

Query: 617 DGLPSRGLPFKHGDILHVTNASDDEWWQARRVLGDNEDEQIGIVPSKRRWERKMRARDRS 676
      GLPS+GL FK+GDILHV NASDDEWWQARRV+ + + E++G++PSKRR ERK RAR ++
Sbjct: 553 SGLPSQGLSFKYGIDILHVINASDDEWWQARRVMLEGDSEEMGVIPSKRRVERKERARLKT 612

Query: 677 VKFQGHAAANNLDKQSTLDRKKKNFTFSRKFPFMSRDEKNEGDSDQEPNGVVSSTSEI 736
      VKF ++ K S D++KK+F FSRKFPF K++++ ++ SD E +
Sbjct: 613 VKFNAKPGVIDS--KGSFNDKRKKS FFSRKFPFYKNEQSEQETS DPE-----RGQE 663

Query: 737 DIXXXXXXXXXXXXXXXXXXVLSYEAVQRLSINYTRPVIILGPLKDRINDDLISEY PDKFG 796
      D+ +LSYE V R INYTRPVIILGP+KDRINDDLISE+PDKFG
Sbjct: 664 DL-----ILSYEPVTRQEINYTRPVIILGPMKDRINDDLISEFPDKFG 706


Query: 797 SCVPHTTRPKREYVDGRDYHFVSSREQMERDIQNHLEAGQYNDNLYGTSVASVREVA 856
      SCVPHTTRPKR+YEVDGRDYHFV SREQME+DIQ H FIEAGQYNDNLYGTSV SVR VA
Sbjct: 707 SCVPHTTRPKRDYVDGRDYHFVISREQMEKDIQEHKFIEAGQYNDNLYGTSVQSVRFVA 766

Query: 857 EKGKHCILDVSGNAIKRLQVAQLYPVAVFIKPKSVDSVMEMNRRMTEEQAKKTYERA IKM 916
      E+GKHCILDVSGNAIKRLQVAQLYP+A+FIKP+S++S+MEMN+R+TEEQAKKTY+RAIK+
Sbjct: 767 ERGKHCILDVSGNAIKRLQVAQLYPIAIFIKPRSLESLEMMNKRLEEEQAKKTYDRAIKL 826

Query: 917 EQEFG EYFTGVVQGD TIEEIYSKVKS MIWSQSGPTI WVPSKESL 960
      EQEFG EYFT +VQGD T+E+IY++ K +I QSGP IW+PSKE L
Sbjct: 827 EQEFG EYFTAIVQGD TLEDIYNQCKLVIEEQSGPFIWIPSKEKL 870
Score = 197 bits (502), Expect = 7e-49
Identities = 111/221 (50%), Positives = 140/221 (63%), Gaps = 24/221 (10%)
  
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(SEQ ID NO:259)

(SEQ ID NO:292)



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Query: 23 SLFNLDVSGDD-SWLYEDIQLERGN SGLGFSIAGGTDNPHIGTDTSIYITKLISGGAAA 81
      +L + VNG + + +E+I LERGN SGLGFSIAGGTDNPHIG D I+ITK+I GGAAA
Sbjct: 80 TLDTIPYVNGTEIEYEFEEITLERGN SGLGFSIAGGTDNPHIGDDPGIFITKIIPGGAAA 139

Query: 82 ADGRLXXXXXXXXXXXXXXXXXPHASAVDALKKAGNVVVLHVVRKXXXXXXXXXXXXXXXXX 141
      DGRL H+ AV+ALK+AG++ +L+V+R+
Sbjct: 140 EDGRLRVNDCILRVNEVDVSEVSHSKAVEALKEAGSIARLYVRRRRPILET----- 190
  
```

(SEQ ID NO:293)

(SEQ ID NO:294)

MARKED-UP VERSION

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Query: 142 XXXXXXXXXXKVEIDLKVGKGLGFSIAGGIGNQHIPGDNGIYVTKLTDGGRAQVDGRLS 201
 V+EI L KG KGLGFSIAGG+GNQHIPGDN IYVTK+ DGG AQ DGRL
 Sbjct: 191 -----VVEIKLFKGPGLGFSIAGGVGNQHIPGDNSIYVTKIIDGGAAQKDGRLQ 240

Query: 202 IGDKLIAVRTNGSEKNLENVTHELAVATLKSITDKVTLIIG 242
 +GD+L+ V + +LE VTHE AVA LK+ ++ V L +G
 Sbjct: 241 VGDRLLMV----NNYSLEEVTHEEAVAILKNTSEVVYLKVG 277
 Score = 66.2 bits (160), Expect = 3e-09
 Identities = 40/125 (32%), Positives = 64/125 (51%), Gaps = 11/125 (8%)



Query: 448 SPQPRQPGSRYASTNVLAAPPGTPRAVSTEDITREPTITIQKGPQGLGFNIVGGEDGQ 507
 SP P +T+ L +P V+ +I E IT+++G GLGF+I GG D
 Sbjct: 65 SPLKASPAPIIVNTDLDLTIP-----YVNGTEIEYEFEEITLERGNSGLGFSIAGGTDNP 119

Query: 508 -----GIYVSFILAGGPADLGSSELKRGDQLLSVNNVNLTHATHEEAAQALKTSGGVVTL 561
 GI+++ I+ GG A L+ D +L VN V+++ +H +A +ALK +G + L
 Sbjct: 120 HIGDDPGIFITKIIPGAAAEDGRLRVNDCILRVNEVDVSEVSHSKAVEALKEAGSIARL 179

Query: 562 LAQYR 566
 + R
 Sbjct: 180 YVRRR 184
 Score = 65.5 bits (158), Expect = 5e-09
 Identities = 38/81 (46%), Positives = 47/81 (57%), Gaps = 6/81 (7%)



Query: 487 ITIQKGPQGLGFNIVGGEDGQ-----GIYVSFILAGGPADLGSSELKRGDQLLSVNNVNL 540
 I + KGP+GLGF+I GG Q IYV+ I+ GG A L+ GD+LL VNN +L
 Sbjct: 194 IKLFKGPGLGFSIAGGVGNQHIPGDNSIYVTKIIDGGAAQKDGRLQVGDRLLMVNNYSL 253

Query: 541 THATHEEAAQALKTSGGVVTL 561
 THEEA LK + VV L
 Sbjct: 254 EEVTHEEAVAILKNTSEVVYL 274
 Score = 50.8 bits (120), Expect = 1e-04
 Identities = 33/87 (37%), Positives = 48/87 (54%), Gaps = 10/87 (11%)



Query: 154 EIDLKVGKGLGFSIAGGIGNQHIPGDNGIYVTKLTDGGRAQVDGRLSIGDKLIAVRTNG 213
 ++ L KG GLGF+I GG + GI+V+ + GG A + G L GD+++V NG
 Sbjct: 421 KVVHLKGSTGLGFNIVGGEDGE-----GIFVFSFILAGGPADLSGELQRGDQILSV--NG 472

Query: 214 SEKNLENVTHELAVATLKSITDKVTLI 240
 + L +HE A A LK VT+I
 Sbjct: 473 ID--LRGASHEQAAAALKGAGQTVTII 497
 Score = 41.2 bits (95), Expect = 0.10
 Identities = 24/81 (29%), Positives = 36/81 (43%), Gaps = 6/81 (7%)



Query: 41 IQLERGNISGLGFSIAGGTDNPHIGTDTSIYITKLISGGAAAADGRLXXXXXXXXXXXXX 100
 + L +G+++GLGF+I GG D I+++ +++GG A G L
 Sbjct: 422 VVLHKGSTGLGFNIVGGEDG-----EGIFVFSFILAGGPADLSGELQRGDQILSVNGIDL 475

Query: 101 XXXPHASAVDALKKAGNVVKL 121
 H A ALK AG V +
 Sbjct: 476 RGASHEQAAAALKGAGQTVTI 496

(SEQ ID NO:295)

(SEQ ID NO:296)

(SEQ ID NO:297)

(SEQ ID NO:298)

(SEQ ID NO:299)

(SEQ ID NO:300)

(SEQ ID NO:301)

(SEQ ID NO:302)

CLUSTAL W (1.82) sequence alignment

(SEQ ID NO:261)
(SEQ ID NO:303)

Hu-Dlg1	---MPVRKQDTQRALHLLLEEYRSKLSTQEDRQLRSSIERVINIFQSNLFQ-ALIDIQEYF	56
Hu-Dlg4	---MSQRPRAPRSALWLLAPPLLRWAPP-----LLTVLHSDLFQ-ALLDILDYY	45
Hu-Dlg2	---MFFACYCALRTNVKKYRYQDEAPHDHS-----LPRLTHEVRGP-ELVHVSEK-	47
Hu-Dlg3	MHKHQHCCKCEPECYEVTRLAALRRLEPPGYG----DWQVPDPYPGPGGGNGASAGYGGYS	55
Dm-Dlg1	---MTTRKK-----KRDGG-----	11
Hu-Dlg5	-----	
Hu-Dlg1	EVTLLDNPKCIDRSKPSEPIQPVTWEISSLPSSSTVTSETLPSSLSPSVEKYRYQDEPTP	116
Hu-Dlg4	EASLSES-----QKYRYQDEPTP	63
Hu-Dlg2	NLSQIEN-----VHGYYVLQSHISP	66
Hu-Dlg3	SQTLP SQAG-----ATPTPRTKAKLIP	77
Dm-Dlg1	-----	
Hu-Dlg5	-----	
Hu-Dlg1	PQEHISPPQITNEVIGPELVHVSEKNLSEIENVHGFVSHSHSPIKPTAEAVLSPSPPTVPVI	176
Hu-Dlg4	PLEHSP-----AHLPN-----	74
Hu-Dlg2	LK-----	68
Hu-Dlg3	TGRDVG-----PVPLKPVPGK-----	93
Dm-Dlg1	-----	
Hu-Dlg5	-----	
Hu-Dlg1	PVLPVPAENTVILPTIPQANPPPVLVNDSLETTP---TYVNGTDADYEYEEITLERGNSG	233
Hu-Dlg4	-----QANSPPVIVNTDTLEAPGYELQVNGTEGEMEYEEITLERGNSG	117
Hu-Dlg2	-----ASPAPIIVNTDTLDITP---YVNGTEIEYEFEEITLERGNSG	107
Hu-Dlg3	-----STPKLNGSGPSWWPECTCTNRDWYEQVNGSDGMFKYEEIVLERGNSG	140
Dm-Dlg1	-----GSGGGFIKKVSSLFNLD---SVNGDD-SWLIEDIQLERGNSG	49
Hu-Dlg5	-----MRATHGSNSLPSSARLGSSSN	21
	: *	
Hu-Dlg1	LGFSIAGGTNDNPHIGDDSSIFITKIIITGGAAAQDGRLRVNDICILQVNEVDVDRVTHSKAV	293
Hu-Dlg4	LGFSIAGGTNDNPHIGDDPSIFITKIIIPGGAAAQDGRLRVNDISILFVNEVDVREVTHSAAV	177
Hu-Dlg2	LGFSIAGGTNDNPHIGDDPGIFITKIIIPGGAAEDGRLRVNDICILRVNEVDVSEVSHSKAV	167
Hu-Dlg3	LGFSIAGGIDNPVHPDDPGIFITKIIIPGGAAAMDGR LGVNDCVLRVNEVEVSEVVHSHRAV	200
Dm-Dlg1	LGFSIAGGTNDNPHIGTDTSIYITKLI SGGAAAADGR LSINDI IVS VNDVSVDVPHASAV	109
Hu-Dlg5	LQFKAER-IKIPSTPRYPRSVVGSER--GSVSHSECSTPPQSPLNIDLTLSSCSQSQT SAS	78
	* * . . * : . * : : : . . : *	
Hu-Dlg1	EALKEAGSIVRLYVKRRK-----PVS-----EKIMEIKLIKGP KGLGFSI	333
Hu-Dlg4	EALKEAGSIVRLYVMRK-----PPA-----EKMVEIKLIKGP KGLGFSI	217
Hu-Dlg2	EALKEAGSIARLYVRRRR-----PIL-----ETVVEIKLFKGPKGLGFSI	207
Hu-Dlg3	EALKEAGPVVRLVRRRQ-----PPP-----ETIMEVNLLKGPKGLGFSI	240
Dm-Dlg1	DALKKAGNVVKLHVKRKR-GTATT PAAGSAAGDARD SAASGPKVIEIDL VKGGKGLGFSI	168
Hu-Dlg5	TLPRIAVNPASLGERRKDR--PYV-----EEP RHVKVQGKSEPLGISI	119
	: * . * *: . : : * : ** :	
Hu-Dlg1	AGGVGNQH I PGDNSI YVTKI IEGGA AHKD GRL QIGDK LLAVNN---VCLEEVTHEEA VT	389
Hu-Dlg4	AGGVGNQH I PGDNSI YVTKI IEGGA AHKD GRL QIGDK ILAVNS---VGLED VMHEDA VA	273
Hu-Dlg2	AGGVGNQH I PGDNSI YVTKI IDGGA AQD GR LQVGD RLLMVNN---YSLEEVTHEEA VA	263
Hu-Dlg3	AGGIGNQH I PGDNSI YITKI IEGGA AQD GR LQIGD RL LAVNN---TNLQDVN THEEA VA	296
Dm-Dlg1	AGGIGNQH I PGDNGI YVT KL TDG GRA QVD GR LS IGDK LI AV RTN NG EKD NV TH EA VA	228
Hu-Dlg5	VSGE-----KGGIYVSKVT VG SI AHQA G-L EYG DQL LE FNG---IN LR SAT EQQA RL	167
	. *. . . **::*: *. *: *. *. **:::.. *... : *	
Hu-Dlg1	ALKNTSDFVYLKVAKPTSMYMN DGYA-----	415
Hu-Dlg4	ALKNTYDVVYLKVAKPSNAYLSDSYA-----	299
Hu-Dlg2	ILKNTSEVVYLKVGNPTTIYMTDPYG-----	289
Hu-Dlg3	SLKNTSDMVYLKVAKPGSLHLNDGYA-----	322
Dm-Dlg1	TLKSITDKVTLLIIGKTQHLTISASGGGGGGLSSGQLSQSQSQLATSQSQSQVHQQQHAT	288
Hu-Dlg5	IIGQQCDTITILAQYNPHVHQLSSH-----	193
	: . : : :	
Hu-Dlg1	-----	
Hu-Dlg4	-----	
Hu-Dlg2	-----	
Hu-Dlg3	-----	
Dm-Dlg1	PMVNSQSTGALNSMGQT VVDS PSI POAAAAVA AANA SASASV IASNNTI SN TTTVT TVTA	34

(SEQ ID NO:267)
(SEQ ID NO:304)
(SEQ ID NO:303)
(SEQ ID NO:305)
(SEQ ID NO:259)
(SEQ ID NO:306)

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Hu-Dlg5 -----

Hu-Dlg1 -----PP-----DITNSSSQVDNHVS-----PSSFLG----- 438
Hu-Dlg4 -----PP-----DITTSYSQHLNEIS-----HSSYLGTD-----YP 326
Hu-Dlg2 -----PP-----DITHSYSPPMENHLL-----SGNNGTLE-----YK 316
Hu-Dlg3 -----PP-----DYASTFTALADNHIS-----HNSSLGYLGAVESKVS 356
Dm-Dlg1 TATASNDSSKLPPSLGANSSISISNSNSNSNNINNINSINNNSSSSSSTTATVAAATP 408
Hu-Dlg5 -----RSSSHLDPAAGTHSTLQ-----GSGTTTPEHPSVIDPLM 226
      : : .. ..

Hu-Dlg1 --QTPASPARYSPVSKAVLGDEITR----- 462
Hu-Dlg4 TAMTPTSPRRYSPVAKDLLGEEDIPR----- 352
Hu-Dlg2 TSLPPISPGRYSPIPKHMLVDDDYTRPPEPVYSTVNKLCDKSPRHYSPVECDKSFLLS 376
Hu-Dlg3 PAPPQVPPTRYSPIPRHMLAEEDFTR----- 382
Dm-Dlg1 TAASAAAAAASSPPANSFYNNASMPALPVESNQTNNRSQSPQPRQPGSRVASTN----- 462
Hu-Dlg5 EQDEGPSTPPAKQSSSRIAGDANKKT----- 252
      . . . . : .

Hu-Dlg1 -----EPRKVVLHRGSTGLGFNIV 481
Hu-Dlg4 -----EPRRIVIHRRGSTGLGFNIV 371
Hu-Dlg2 APYSHYHLGLLPDSEMTSHSQHSTATRQPSMTLQRAVSLGEGPRKVVLHKGSTGLGFNIV 436
Hu-Dlg3 -----EPRKIILHKGSTGLGFNIV 401
Dm-Dlg1 -----VLAAVPPGTPRAVSTEDITREPTITIQKGPQGLGFNIV 501
Hu-Dlg5 -----LEPRVVFIIKKSQLELGVHLC 272
      *** : : : . ** : :

Hu-Dlg1 GGEDGEGIFISFILAGGPADLSGELRKGDRIISVNSVDLRAASHEQAAAAALKNAGQAVTI 541
Hu-Dlg4 GGEDGEGIFISFILAGGPADLSGELRKGDQILSVNGVDLRNASHEQAAIALKNAGQTVTI 431
Hu-Dlg2 GGEDGEGIFVSVFILAGGPADLSGELQRGDQILSVNGIDLRGASHEQAAAAALKGAGQTVTI 496
Hu-Dlg3 GGEDGEGIFVSVFILAGGPADLSGELRRGDRILSVNGVNLNRNATHEQAAAAALKRAGQSVTI 461
Dm-Dlg1 GGEDGQGIYVSFILAGGPADLSGELKRGDQLLSVNNVNLTHATHEEAAQALKTSGGVVTL 561
Hu-Dlg5 GG-NLHGVPVAEVEDDSPAKGPDGLVPGLDILEYGLDVRNKTVEEVYVEMLKPRDGVRL 331
** : .*: : : : . : . * ** : : . : : : : * : : . : . * :

Hu-Dlg1 VAQYRPEEYSRFEAKIHDLEQMMNSSISSGSGSLRTSQKRSLYVRALFDYDKTKDSGLP 601
Hu-Dlg4 IAQYKPEEYSRFEAKIHDLEQMLNSSLGSGTASLRSNPKRGFYIRALFDYDKTKDCGFL 491
Hu-Dlg2 IAQYQPEDYARFEAKIHDLEQMMNHSMSGSGSLRTNQKRSLYVRAMFDYDKSKDSGLP 556
Hu-Dlg3 VAQYRPEEYSRFEAKIHDLEQMMNSSMSGSGSLRTSEKRSLYVRALFDYDRTRDSCLP 521
Dm-Dlg1 LAQYRPEEYNRFEARIQELKQQAALGAGGSGT-LLRTTQKRSLYVRALFDYDPNRDDGLP 620
Hu-Dlg5 KVQYRPEEFTKAG-----LPGDSFYIRALYDR-----LADV 363
      .*: : : : : : . : : : : *

Hu-Dlg1 SQGLNFKFGDILHVINASDD---EWWQARQVTPDGESDEVGVIPSKRRVEKKERARLKT 658
Hu-Dlg4 SQALSFRFGDVLHVIDASDE---EWWQARRVHSDSETDDIGFIPSKRRVERREWSRLKAK 548
Hu-Dlg2 SQGLSFKYGDILHVINASDD---EWWQARRVMLEGDSEEMGVIPSKRRVERKERARLKT 613
Hu-Dlg3 SQGLSFSEYGDILHVINASDD---EWWQARLVTPHGESEQIGVIPSARRVEKKERARLKT 578
Dm-Dlg1 SRGLPFFKHGDILHVTNASDD---EWWQARRVLGDNEDEQIGVIPSARRWERKMRARDRSV 677
Hu-Dlg5 EQELSFKKDDILYVDDTLPGTFGSWMAWQLDENAQKIQRGQIPSKYVMDQEFRRRLSMS 423
.: * * .*: : * : : * * : . : : * : *** : : . *

Hu-Dlg1 KFNSKT-----RDKGQSFNDKRKKNLFSRKFPFYKNKDQSEQETSDADQH----- 703
Hu-Dlg4 DWG----- 551
Hu-Dlg2 KFNAKPGVI--DSKGSFNDKRKKSFIKSRKFPFYKNKEQSEQE----- 654
Hu-Dlg3 KFHARTGMI--ESNRDFPGLSDDYY----- 601
Dm-Dlg1 KFQGHAAANNLDKQSTLDRKKKNFTFSRKFPFMKSRDEKNEGSDQEPNGVVSSTSEID 737
Hu-Dlg5 EVKDDNSATKTLSAAARRSFFRRKHKHKSRSKDGKDLLALDAFS----- 468
      .

Hu-Dlg1 VTSNASDSESSYRGQEEYVLSYEPVNQQEVNYTRPVIILGPMKDRINDDLISEFPDKFGS 763
Hu-Dlg4 -----SSSGSQGREDSVLSYETVTQMEVHYARPIIILGPTKDRANDLLSEFPDKFGS 604
Hu-Dlg2 -----TSDPERGQEDLILSYEPVTRQEIYNYTRPVIILGPMKDRINDDLISEFPDKFGS 707
Hu-Dlg3 -----GAKNLKGQEDAILSYEPVTRQEIHYARPVIILGPMKDRVNDLISEFPDKFGS 654
Dm-Dlg1 INNVDNNQSNQEPQSEENVLSYEAQRLSINYTRPVIILGPLKDRINDDLISEYDPDKFGS 797
Hu-Dlg5 -----SDSIPLFEDSVSLAYQRVQKVDCTALRPVLIILGPLLDVVKEMLVNEAPGKFCR 521
      . : . * : : * : . * : : * : * : * : * : * : * : * : *

Hu-Dlg1 CVPHTTRPKRDYEVDRDYHFVTSREQMEKDIQEHKFIAGQYNNHLYGTSVQSVREVAG 823
Hu-Dlg4 CVPHTTRPKREYIDGRDYHFVSSREKMEKDIQAHKFIAGQYNSHLYGTSVQSVREVAE 664
Hu-Dlg2 CVPHTTRPKRDYEVDRDYHFVTSREQMEKDIQEHKFIAGQYNDNLYGTSVQSVRFVAE 767
Hu-Dlg3 CVPHTTRPRDNEVDGQDYHFVVSREQMEKDIQDNKFIAGQFNDNLYGTSIQSVRAVAE 714
Dm-Dlg1 CVPHTTRPKREYEVDRDYHFVSSREQMERDIQNHLEAGQYNDNLYGTSVASVREVAE 857
Hu-Dlg5 CPLEVMK-----ASQQAIERGVKDCLFVDYKRRSGHFDVTTVASIXEITE 566
* . . : * : : * : : * : : * : : * : : * : : * : :

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YFV
16/19

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